

## General

### Guideline Title

Bacterial sepsis following pregnancy.

### Bibliographic Source(s)

Royal College of Obstetricians and Gynaecologists (RCOG). Bacterial sepsis following pregnancy. London (UK): Royal College of Obstetricians and Gynaecologists (RCOG); 2012 Apr. 21 p. (Green-top guideline; no. 64b). [54 references]

### Guideline Status

This is the current release of the guideline.

## Recommendations

### Major Recommendations

*In addition to these evidence-based recommendations, the guideline development group also identifies points of best clinical practice in the original guideline document.*

Classification of evidence levels (1++ to 4) and grades of recommendations (A-D) are defined at the end of the "Major Recommendations" field.

What Should Prompt Recognition of Sepsis in the Puerperium?

D - All health professionals should be aware of the symptoms and signs of maternal sepsis and critical illness and of the rapid, potentially lethal course of severe sepsis and septic shock. Suspicion of significant sepsis should trigger urgent referral to secondary care.

Clinical signs suggestive of sepsis include one or more of the following: pyrexia, hypothermia, tachycardia, tachypnoea, hypoxia, hypotension, oliguria, impaired consciousness and failure to respond to treatment. These signs, including pyrexia, may not always be present and are not necessarily related to the severity of sepsis.

The common symptoms of sepsis in the puerperium include fever, diarrhoea, vomiting, abdominal pain, generalised maculopapular rash (staphylococcal or streptococcal sepsis), offensive vaginal discharge and signs of infection in caesarean wounds. Agonising pain out of proportion to the clinical signs suggests a deep infection, and necrotising fasciitis/myositis must be considered. [Evidence level 3]

Table 2 in the original guideline document details common symptoms of sepsis in the puerperium. See Appendix 1 in the original guideline document for a definition and classification of toxic shock syndrome.

What Investigations Should Be Performed?

D - Blood cultures are the key investigation and should be obtained prior to antibiotic administration; however, antibiotic treatment should be started without waiting for microbiology results.

D - Serum lactate should be measured within 6 hours of the suspicion of severe sepsis to guide management. Serum lactate  $\geq 4$  mmol/l is indicative of tissue hypoperfusion.

D - Any relevant imaging studies should be performed promptly in an attempt to confirm the source of infection. This could include a chest X-ray, pelvic ultrasound scan or computed tomography scan if pelvic abscess is suspected.

Blood cultures and other samples taken should be guided by clinical suspicion of focus of infection, such as throat swabs, mid-stream urine, high vaginal swab, placental swabs, sputum, cerebrospinal fluid, epidural site swab, caesarean section or episiotomy site wound swabs and expressed breast milk, and should ideally be obtained prior to starting antibiotic therapy as the results may become uninformative within a few hours of commencing antibiotics. Antibiotics should be given as soon as possible. Results of laboratory tests should be checked and recorded regularly and the medical microbiologist consulted to ensure specimens are processed appropriately and results communicated directly to the clinician at the earliest opportunity. Gram stain, culture results and sensitivities should be used to tailor antimicrobial therapy.

If diarrhoea is particularly offensive following antimicrobial therapy, a stool sample should be submitted for *Clostridium difficile* toxin testing. A history of diarrhoea warrants routine culture (e.g., *Salmonella*, *Campylobacter*). The laboratory should be informed if there is a clinical indication for investigations for unusual pathogens such as *Listeria monocytogenes* (consumption of soft cheese or cured meats) or if there is a history of foreign travel (parasites, typhoid or cholera).

Bacterial numbers may be scanty or not seen on initial Gram staining of swabs, fluids, or debrided tissue. However, organisms seen on Gram staining will guide empirical prescribing. A paucity of leucocytes and the presence of Gram-positive cocci in chains indicate streptococcal infection. 'Mixed organisms' (i.e., mixed Gram- negative and -positive organisms) would suggest the possibility of gut organisms, including anaerobes, as part of a synergistic infection.

Diagnostic criteria for sepsis are available in Appendix 2 of the original guideline document (in the absence of specific criteria for women in the puerperium).

Table 3 in the original guideline indicates tasks which should be performed within the first 6 hours of the identification of severe sepsis.

How Should Sepsis in the Puerperium Be Managed?

*Which Antibiotics Should Be Used?*

D - Administration of intravenous broad-spectrum antibiotics within 1 hour of suspicion of severe sepsis, with or without septic shock, is recommended as part of the Surviving Sepsis resuscitation care bundle.

D - If genital tract sepsis is suspected, prompt early treatment with a combination of high-dose broad spectrum intravenous antibiotics may be life saving.

Antibiotic therapy should be guided by the Gram stain of any aspirate or biopsy; however, in practice the patient is usually so sick there is no time to wait, hence initial empirical prescribing of broad-spectrum antibiotics is essential. Intravenous broad-spectrum antibiotics should be given within 1 hour of suspicion of severe sepsis. [Evidence level 4]

Information on antimicrobials which may aid in guiding choice is given in Table 4 in the original guideline, but hospital guidelines differ and local guidance should be followed since the incidence of resistant organisms varies throughout the UK. The decision as to which antimicrobials to include in the hospital formulary and maternity unit guidelines for severe sepsis in the puerperium should be agreed by clinicians and the hospital microbiologist.

National guidelines for the management of community-acquired pneumonia, Panton-Valentine leukocidin (PVL)-producing *Staphylococcus aureus* and methicillin-resistant *S. aureus* (MRSA)-associated infections should be consulted where necessary. [Evidence level 4]

*What Is the Role of Intravenous Immunoglobulin (IVIG)?*

D - IVIG is recommended for severe invasive streptococcal or staphylococcal infection if other therapies have failed.

IVIG is available from the blood transfusion department. All commercial brands of IVIG available in the UK contain antibodies to streptococcal and staphylococcal exotoxins. Actual administration of IVIG should be through a blood warming device and hospital guidelines/protocols for replacement therapy in haematology patients may be used. However, when faster replacement is necessary in severely ill patients, the Mount Sinai hospital protocol may be helpful. [Evidence level 4]

## What Are the Neonatal Issues If Sepsis Develops in the Puerperium?

D - The baby is especially at risk of streptococcal and staphylococcal infection during birth and during breastfeeding. The umbilical area should be examined and a paediatrician consulted in the event of sepsis in the puerperium.

The infant of a mother colonised with Group B Streptococci should be managed as per RCOG Green-top Guideline No.36: *Prevention of early onset neonatal group B streptococcal disease*. [Evidence level 4]

### Definitions:

#### Classification of Evidence Levels

1++ High-quality meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a very low risk of bias

1+ Well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias

1– Meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a high risk of bias

2++ High-quality systematic reviews of case-control or cohort studies or high-quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal

2+ Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal

2– Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal

3 Non-analytical studies, e.g. case reports, case series

4 Expert opinion

#### Grades of Recommendations

A - At least one meta-analysis, systematic review or randomised controlled trial rated as 1++ and directly applicable to the target population; *or*

A systematic review of randomised controlled trials or a body of evidence consisting principally of studies rated as 1+ directly applicable to the target population and demonstrating overall consistency of results

B - A body of evidence including studies rated as 2++ directly applicable to the target population, and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 1++ or 1+

C - A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 2++

D - Evidence level 3 or 4; *or*

Extrapolated evidence from studies rated as 2+

Good Practice Point - Recommended best practice based on the clinical experience of the guideline development group

## Clinical Algorithm(s)

None provided

## Scope

## Disease/Condition(s)

Bacterial sepsis following pregnancy

Note: Sepsis in pregnancy is covered by a parallel guideline. Sepsis arising owing to viral or parasitic agents is outside the scope of this guideline. This guideline excludes mild to moderate illness in primary care.

## Guideline Category

Diagnosis

Evaluation

Management

Risk Assessment

Treatment

## Clinical Specialty

Family Practice

Infectious Diseases

Internal Medicine

Obstetrics and Gynecology

## Intended Users

Advanced Practice Nurses

Hospitals

Nurses

Physician Assistants

Physicians

## Guideline Objective(s)

To provide guidance on the management of sepsis in the puerperium (i.e., sepsis developing after birth until 6 weeks postnatally), in response to the findings of the Centre for Maternal and Child Enquiries (CMACE) Eighth Report on Confidential Enquiries into Maternal Deaths in the United Kingdom

## Target Population

Women in the puerperium (i.e., within 6 weeks of giving birth) with suspected or diagnosed bacterial sepsis in primary or secondary care

## Interventions and Practices Considered

Diagnosis/Evaluation/Risk Assessment

1. General history, physical examination, and clinical assessment to identify source of sepsis
2. Recognition of signs of maternal sepsis with urgent referral to secondary care
3. Monitoring of woman with sepsis and all vital signs (including temperature, pulse rate, blood pressure and respiratory rate) recorded on a Modified Early Obstetric Warning Score (MEOWS) chart
4. Prompt involvement of other specialists (e.g., infectious diseases expert, microbiologist)
5. Infectious disease history/information should be noted.
6. Blood cultures and other samples
7. Serum lactate measurement within 6 hours of the suspicion of severe sepsis
8. Imaging studies (e.g., chest x-ray, pelvic ultrasound, computed tomography scan)
9. Rapid MRSA screening where available

#### Management/Treatment

1. Administration of intravenous broad-spectrum antibiotics within 1 hour of suspicion of severe sepsis
2. Prompt early treatment with a combination of high-dose broad-spectrum intravenous antibiotics for suspected genital tract sepsis
3. Intravenous immunoglobulin (IVIG) for severe invasive streptococcal or staphylococcal infection if other therapies have failed
4. Early hospital referral
5. Admission to intensive care unit when indicated
6. Managing drug-misusing women
7. Consideration of infection control issues
8. Umbilical area examination and paediatrician consult
9. Indications for family/staff prophylaxis
10. Prevention and early detection of sepsis

## Major Outcomes Considered

- Incidence of sepsis in the puerperium
- Effectiveness of treatment
- Progression of disease
- Incidence of maternal death
- Adverse effects of treatment
- Transmission of infection

## Methodology

### Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

### Description of Methods Used to Collect/Select the Evidence

This Royal College of Obstetricians and Gynaecologists (RCOG) guideline was developed in accordance with standard methodology for producing RCOG Green-top Guidelines (see the "Availability of Companion Documents" field). The Cochrane Database of Systematic Reviews, DARE, EMBASE, Medline and PubMed (electronic databases) were searched for relevant randomised controlled trials, systematic reviews and meta-analyses. The search was restricted to articles published between 1980 and May 2011. Search terms included: 'postpartum sepsis', 'postpartum infection', 'septic shock, postpartum', 'puerperal sepsis', 'puerperal pyrexia', 'puerperal fever', 'genital tract sepsis', 'bacterial sepsis', 'toxic shock', 'activated protein C and postpartum', '*Streptococcus* infection and puerperium', 'group A *streptococcus*', '*Streptococcus pyogenes*', 'beta haemolytic *Streptococcus* and puerperium'. The search was limited to humans and the English language. The National Library for Health and the National Guidelines Clearing House were also searched for relevant guidelines and reviews. Studies relevant to the scope of the guideline were selected by the members of the guideline development group.

## Number of Source Documents

Not stated

## Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

## Rating Scheme for the Strength of the Evidence

Classification of Evidence Levels

1++ High-quality meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a very low risk of bias

1+ Well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias

1– Meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a high risk of bias

2++ High-quality systematic reviews of case-control or cohort studies or high-quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal

2+ Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal

2– Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal

3 Non-analytical studies, e.g. case reports, case series

4 Expert opinion

## Methods Used to Analyze the Evidence

Systematic Review

## Description of the Methods Used to Analyze the Evidence

Reviewing and Grading of Evidence

Once the evidence has been collated for each clinical question it needs to be appraised and reviewed (refer to section 3 in "Development of RCOG Green-top guidelines: producing a clinical practice guideline" for information on the formulation of the clinical questions; see the "Availability of Companion Documents" field). For each question, the study type with least chance of bias should be used. If available, randomised controlled trials (RCTs) of suitable size and quality should be used in preference to observational data. This may vary depending on the outcome being examined.

The level of evidence and the grade of the recommendations used in this guideline originate from the guidance by the Scottish Intercollegiate Guidelines Network (SIGN) Grading Review Group, which incorporates formal assessment of the methodological quality, quantity, consistency, and applicability of the evidence base. The methods used to appraise individual study types are available from the SIGN Web site ([www.sign.ac.uk/methodology/checklists.html](http://www.sign.ac.uk/methodology/checklists.html)). An objective appraisal of study quality is essential, but paired reviewing by guideline leads may be impractical because of resource constraints.

Once evidence has been collated and appraised, it can be graded. A judgement on the quality of the evidence will be necessary using the grading system (see the "Rating Scheme for the Strength of the Evidence" field). Where evidence is felt to warrant 'down-grading', for whatever reason, the rationale must be stated. Evidence judged to be of poor quality can be excluded. Any study with a high chance of bias (either 1– or 2–) will be excluded from the guideline and recommendations will not be based on this evidence. This prevents recommendations being based on poor-quality RCTs when higher-quality observational evidence is available.

# Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

## Description of Methods Used to Formulate the Recommendations

### Guideline Development

The development of guidelines involves more than the collation and reviewing of evidence. Even with high-quality data from systematic reviews of randomised controlled trials, a value judgement is needed when comparing one therapy with another. This will therefore introduce the need for consensus.

Royal College of Obstetricians and Gynaecologists (RCOG) Green-top guidelines are drafted by nominated developers, in contrast to other guideline groups such as the National Institute for Health and Clinical Excellence (NICE) and the Scottish Intercollegiate Guidelines Network (SIGN), who use larger guideline development groups. Equally, in contrast to other guideline groups, the topics chosen for development as Green-top guidelines are concise enough to allow development by a smaller group of individuals.

In agreeing the precise wording of evidence-based guideline recommendations and in developing consensus-based 'good practice points', the Guidelines Committee (GC) will employ an informal consensus approach through group discussion. In line with current methodologies, the entire development process will follow strict guidance and be both transparent and robust. The RCOG acknowledges that formal consensus methods have been described, but these require further evaluation in the context of clinical guideline development. It is envisaged that this will not detract from the rigor of the process but prevent undue delays in development.

## Rating Scheme for the Strength of the Recommendations

### Grades of Recommendations

A - At least one meta-analysis, systematic review or randomised controlled trial rated as 1++ and directly applicable to the target population; *or*

A systematic review of randomised controlled trials or a body of evidence consisting principally of studies rated as 1+ directly applicable to the target population and demonstrating overall consistency of results

B - A body of evidence including studies rated as 2++ directly applicable to the target population, and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 1++ or 1+

C - A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 2++

D - Evidence level 3 or 4; *or*

Extrapolated evidence from studies rated as 2+

Good Practice Point - Recommended best practice based on the clinical experience of the guideline development group

## Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

## Method of Guideline Validation

External Peer Review

Internal Peer Review

## Description of Method of Guideline Validation

Following discussion in the Guidelines Committee (GC), each Green-top guideline is formally peer reviewed. At the same time, the draft guideline is published on the Royal College of Obstetricians and Gynaecologists (RCOG) Web site for further peer discussion before final publication.

All comments will be collated by the RCOG and tabulated for consideration by the guideline leads. Each comment will require discussion. Where comments are rejected then justification will need to be made. Following this review, the document will be updated and the GC will then review the revised draft and the table of comments.

Once the GC signs-off on the guideline, it is submitted to the Standards Board for approval before final publication.

## Evidence Supporting the Recommendations

### Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

## Benefits/Harms of Implementing the Guideline Recommendations

### Potential Benefits

Appropriate management of bacterial sepsis following pregnancy to improve maternal survival rates

### Potential Harms

- Treatment with any antimicrobial can cause allergic reactions, including skin rashes. However, it should be remembered that, particularly in toxic shock, a maculopapular or blanching erythema may be exotoxin related and not an allergy to the therapy.
- Diarrhoea, particularly if offensive or developing after any antimicrobial therapy, should be sent for *Clostridium difficile* toxin testing. The organism does not infect neonates but can cause up to 30% mortality in mothers if untreated. Pending the result of testing, oral metronidazole or oral vancomycin are used empirically where clinically justified.

## Contraindications

### Contraindications

- The main contraindication to intravenous immunoglobulin (IVIG) use is a congenital deficiency of immunoglobulin A.
- In those with severe penicillin allergy, carbapenems are contraindicated.

## Qualifying Statements

### Qualifying Statements

- These recommendations are not intended to dictate an exclusive course of management or treatment. They must be evaluated with reference

to individual patient needs, resources and limitations unique to the institution and variations in local populations. It is hoped that this process of local ownership will help to incorporate these guidelines into routine practice. Attention is drawn to areas of clinical uncertainty where further research might be indicated.

- The Royal College of Obstetricians and Gynaecologists (RCOG) produces guidelines as an educational aid to good clinical practice. They present recognised methods and techniques of clinical practice, based on published evidence, for consideration by obstetricians and gynaecologists and other relevant health professionals. The ultimate judgement regarding a particular clinical procedure or treatment plan must be made by the doctor or other attendant in the light of clinical data presented by the patient and the diagnostic and treatment options available within the appropriate health services. This means that RCOG Guidelines are unlike protocols or guidelines issued by employers, as they are not intended to be prescriptive directions defining a single course of management. Departure from the local prescriptive protocols or guidelines should be fully documented in the patient's case notes at the time the relevant decision is taken.

## Implementation of the Guideline

### Description of Implementation Strategy

An implementation strategy was not provided.

### Implementation Tools

Audit Criteria/Indicators

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

## Institute of Medicine (IOM) National Healthcare Quality Report Categories

### IOM Care Need

Getting Better

Staying Healthy

### IOM Domain

Effectiveness

Patient-centeredness

Timeliness

## Identifying Information and Availability

### Bibliographic Source(s)

Royal College of Obstetricians and Gynaecologists (RCOG). Bacterial sepsis following pregnancy. London (UK): Royal College of Obstetricians and Gynaecologists (RCOG); 2012 Apr. 21 p. (Green-top guideline; no. 64b). [54 references]

## Adaptation

Not applicable: The guideline was not adapted from another source.

## Date Released

2012 Apr

## Guideline Developer(s)

Royal College of Obstetricians and Gynaecologists - Medical Specialty Society

## Source(s) of Funding

Royal College of Obstetricians and Gynaecologists (RCOG)

## Guideline Committee

Guidelines Committee

## Composition of Group That Authored the Guideline

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## Financial Disclosures/Conflicts of Interest

Conflicts of interest: none declared.

## Guideline Status

This is the current release of the guideline.

## Guideline Availability

Electronic copies: Available from the [Royal College of Obstetricians and Gynaecologists \(RCOG\) Web site](#) .

## Availability of Companion Documents

The following are available:

- Development of RCOG Green-top guidelines: policies and processes. Clinical Governance Advice No 1a. London (UK): Royal College of Obstetricians and Gynaecologists (RCOG); 2006 Nov. 6 p. Electronic copies: Available from the [Royal College of Obstetricians and](#)

Gynaecologists (RCOG) Web site .

- Development of RCOG Green-top guidelines: producing a scope. Clinical Governance Advice No 1b. London (UK): Royal College of Obstetricians and Gynaecologists (RCOG); 2006 Nov. 4 p. Electronic copies: Available from the [RCOG Web site](#) .
- Development of RCOG Green-top guidelines: producing a clinical practice guideline. Clinical Governance Advice No 1c. London (UK): Royal College of Obstetricians and Gynaecologists (RCOG); 2006 Nov. 13 p. Electronic copies: Available from the [RCOG Web site](#) .
- Development of RCOG Green-top guidelines: consensus methods for adaptation of Green-top guidelines. Clinical Governance Advice No 1d. London (UK): Royal College of Obstetricians and Gynaecologists (RCOG); 2010 Feb. 9 p. Electronic copies: Available from the [RCOG Web site](#) .

In addition, suggested audit topics can be found in section 18 of the [original guideline document](#) .

## Patient Resources

None available

## NGC Status

This NGC summary was completed by ECRI Institute on July 16, 2012. The information was verified by the guideline developer on September 25, 2012.

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